Sleep Medicine 15 (2014) 1547–1553

Contents lists available at ScienceDirect

Sleep Medicine

journal homepage: www.elsevier.com/locate/sleep

Original Article

Impact of sleep-disordered breathing on metabolic dysfunctions in patients with polycystic ovary syndrome

Bidisha Chatterjee, Jyotsna Suri, Jagdish Chander Suri *, Pratima Mittal, Tulsi Adhikari

Vardhaman Mahavir Medical College and Safdarjang Hospital, New Delhi, India

ARTICLE INFO

Article history:
Received 19 March 2014
Received in revised form 10 June 2014
Accepted 30 June 2014
Available online 16 September 2014

Keywords:
Polycystic ovary syndrome (PCOS)
Sleep-disordered breathing (SDB)
Metabolic dysfunction
Hyperandrogenism
Insulin resistance
Metabolic syndrome

ABSTRACT

Background: Polycystic ovary syndrome (PCOS) is the most common endocrinological disorder among women in the reproductive age group. These women are prone to develop sleep-disordered breathing (SDB) and metabolic disorders. SDB is also associated with metabolic dysfunctions. We hypothesized that SDB is an independent risk factor contributing to metabolic dysfunctions in women with PCOS.
Methods: Prospective cross-sectional study in which 50 women with PCOS and not on any treatment were selected. They were divided into two groups: Group 1 - PCOS with SDB and Group 2 - PCOS without SDB.
Results: Thirty-three (66%) women with PCOS had SDB. Women in Group 1 had significantly higher systolic blood pressure (SBP) ($P = 0.002$); diastolic blood pressure (DBP) ($P = 0.044$); fasting blood sugar ($P = 0.006$), triglyceride levels ($P = 0.014$) and mean Ferriman-Gallwey score ($P = 0.028$). The HDL was significantly lower in group 1 ($P = 0.006$). In group 1, 42.4% of women had metabolic syndrome ($P < 0.001$). Excessive daytime sleepiness (EDS) was significantly higher in Group 1 ($P = 0.04$). Respiratory distress index significantly correlated positively with waist circumference ($r = 0.551$, $P < 0.001$), SBP ($r = 0.455$, $P = 0.001$), DBP ($r = 0.387$, $P = 0.006$), FBS ($r = 0.524$, $P = 0.000$), homeostatic model assessment ($r = 0.512$, $P = 0.000$), triglycerides ($r = 0.384$, $P = 0.006$), free testosterone ($r = 0.390$, $P = 0.005$), and negatively with HDL ($r = -0.555$, $P < 0.001$).
Conclusion: Women with PCOS and SDB had significantly increased metabolic abnormalities as well as more severe hyperandrogenism. Women with PCOS who have metabolic abnormalities or severe hyperandrogenism should undergo an overnight PSG.

© 2014 Elsevier B.V. All rights reserved.

1. Introduction

Polycystic ovary syndrome (PCOS) is one of the most prevalent (5–10%) gynecological conditions in premenopausal women [1,2]. It is characterized by anovulation, hyperandrogenism, insulin resistance (IR), obesity, and polycystic ovaries [3,4]. The pathogenesis of PCOS is multifactorial, with IR and compensatory hyperinsulinemia being the key factors. Insulin plays a direct role by acting synergistically with luteinizing hormone (LH) to stimulate androgen secretion from theca cells [5]. It also exerts an indirect effect by decreasing the sex hormone-binding globulin (SHBG) production from the liver, further enhancing androgen levels. This androgenic milieu inhibits the selection of dominant follicles, resulting in accumulation of dysfunctional cystic follicles in the ovary and anovulation [6–8].

Though the clinical presentation of most of these patients shows oligomenorrhea, hirsutism, and obesity, it is the metabolic dysfunctions that can have far-reaching, serious consequences. Several studies have shown that women with PCOS are prone to metabolic disorders such as glucose intolerance, type II diabetes mellitus (DM), hypertension, dyslipidemia, and cardiovascular diseases such as hypertension, stroke, and coronary artery disease (CAD) [9–15]. A recent addition to this list of health risks is obstructive sleep apnea (OSA), which has been reported to be higher in women with PCOS in comparison to the general population [6].

Sleep-disordered breathing (SDB) is characterized by repeated episodes of partial or complete cessation of breathing for ≥10 s during sleep. It constitutes a spectrum of disorders of varying severity with intermittent snoring as the mildest and obesity hypoventilation syndrome as the most severe. Heavy snoring, upper airway resistance syndrome, and mild/moderate/severe OSA lie between these two extremes [16]. Prevalence of SDB in women increases with age and body mass index (BMI), and has been reported to be between 2% and 9% [17,18].

The pathogenesis of SDB involves a number of interrelated mechanisms such as anatomically small upper airway and abnormal respiratory control mechanism. The risk of OSA is increased as a function of both total body mass and its distribution. The quantity of visceral fat appears to correlate highly with OSA [19].

* Corresponding author. Vardhaman Mahavir Medical College and Safdarjang Hospital, D-II/153, West Kidwai Nagar, New Delhi 110023, India. Tel.: +91 9810097259; fax: +91 01126190958.
E-mail address: docjcsuri@gmail.com; isda1995@gmail.com (J.C. Suri).

http://dx.doi.org/10.1016/j.sleep.2014.06.023
1389-9457/© 2014 Elsevier B.V. All rights reserved.

Testosterone hormone has also been shown to be a contributory factor in the development of SDB [20]. However, estrogen and progesterone are found to be protective [21].

SDB has several adverse outcomes on the cardiovascular system with increased prevalence of hypertension, CAD, ischemic heart disease (IHD), and stroke. It is also associated with increased prevalence of IR, glucose intolerance, type II DM, and dyslipidemia [22–25].

The overall prevalence of both SDB and PCOS in general population is similar, ranging from 2% to 10%. Both of these conditions have very similar metabolic and cardiovascular complications, indicating a close association between the two.

We hypothesized that SDB is an independent risk factor contributing to the metabolic dysfunctions in women having PCOS. To test this hypothesis, we decided to study the impact of SDB on metabolic dysfunctions in patients with PCOS.

2. Methods

This was a cross-sectional study in which 50 women with PCOS attending the gynecology outpatient department and reproductive endocrinology clinic of Vardhaman Mahavir Medical College (VMMC) and Safdarjung Hospital were randomly selected.

PCOS was defined by the Rotterdam criteria, that is, the presence of any two of the following three features: (1) chronic oligomenorrhea (six or fewer spontaneous menses per year); (2) biochemical or clinical evidence of hyperandrogenism; and (3) polycystic ovaries on ultrasonography [1,26]. Women on any form of treatment for PCOS were not included in the study. Patients with thyroid disorders, hyperprolactinemia, congenital adrenal hyperplasia, smokers, and those with neurological or psychiatric disorders were also excluded from the study.

All women gave written informed consent before participation in this study, which had the approval of the ethics committee of VMMC and Safdarjung Hospital.

2.1. Subject evaluation

Each woman underwent a detailed examination including measurement of height, weight, waist circumference, blood pressure (BP), and general physical and systemic examination. Clinical severity of hirsutism was also determined using Ferriman–Gallwey (FG) score [27]. BMI was calculated and classified according to Indian Standardization [28]. BMI of <18.4 qualified for underweight; 18.5–22.9 was normal; 23–24.9 was overweight; and >25 was obese.

All the women filled out a detailed sleep questionnaire that also included a subjective evaluation of daytime sleepiness (EDS) using the Epworth Sleepiness Scale. Each subject was asked to rate the probability of falling asleep in eight situations on a score of 0–3. The higher the score, the greater was the sleepiness [29–31].

2.2. Biochemical and hormonal assays

A 75 g oral glucose tolerance test was performed on all the patients. Simultaneously, a fasting and postprandial insulin measurement was carried out using enzyme-linked immunosorbent assay. IR was calculated using homeostatic model assessment (HOMA). A value >3.8 was taken as a marker for IR [32,33]. The fasting sample was also subjected to lipid profile including total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglyceride levels. Hormonal assays conducted were serum thyroid-stimulating hormone, serum prolactin, free testosterone, dehydroepiandrostenedione sulfate (DHEAS) and SHBG levels.

Metabolic syndrome (MBS) was defined by the National Cholesterol Education Programme, Adult Treatment Panel (NCEP ACT III) criteria as presence of any three of the following (female-specific range) [34]: FBS ≥110 mg/dL; BP ≥130/85; waist circumference >88 cm; triglyceride ≥150 mg/dL; HDL <50 mg/dL.

2.3. Polysomnography

All 50 patients underwent an overnight polysomnography (PSG), which was performed according to standard laboratory protocol. Data recorded included three-channel electroencephalography (EEG), two-channel electro-oculography, submental and anterior tibialis electromyography, nasal airflow by thermistor, nasal pressure by pressure cannula, thoracic and abdominal efforts by strain gauges, oxygen saturation by pulse oximetry, and tracheal sound recording using microphone attached to the neck. The three EEG channels used were F3M2, C3M2, and O1M2. All signals were simultaneously recorded and stored using a digital PSG system (ALICE 5; Respironics, Inc., Murrysville, PA, USA). A minimum of 7 h of sleep was recorded in each subject. All the PSG records were scored by an experienced sleep medicine consultant.

2.3.1. Definitions of respiratory parameters

- Apnea was diagnosed when there was a drop in the peak thermal sensor excursions by >90% of baseline lasting for ≥10 s. Further, ≥90% of the event duration should have met the amplitude reduction criteria.
- Hypopnea was diagnosed when the nasal pressure signal excursions dropped by ≥50% of the baseline lasting for ≥10 s and were accompanied by a ≥3% drop in oxygen saturation from pre-event baseline or an arousal. Further, ≥90% of the event duration should have met the amplitude reduction criteria.
- Respiratory effort-related arousal (RERA) was defined as an event of increasing respiratory effort or flattening nasal pressure waveform of >10 s followed by an arousal from sleep but which did not meet the criteria for an apnea or hypopnea.
- Respiratory distress index (RDI) was defined as the number of obstructive apneas, hypopneas, and RERAs per hour of sleep. This was calculated by dividing total number of respiratory events with total sleep time in hours.
- SDB was defined as an RDI of ≥5 along with symptoms or an RDI of >15/h with or without associated symptoms. The symptoms include any one of the following: EDS, unrefreshing sleep, gasping or choking, witnessed apneic spells, or nocturia [35].
- Severity of OSA according to RDI was defined as [16,35]: mild OSA, 5 to <15/h; moderate OSA, 15–30/h; severe OSA, >30/h.

The patients were divided into two groups according to their PSG findings. Those with SDB were termed as group 1 and those without SDB were termed as group 2.

The results were tabulated and subjected to statistical analysis. Independent sample *t*-test was used for comparison of continuous variables between the subgroups of PCOS, that is, PCOS with and without SDB. A two-tailed *t*-test was used to calculate the *P* values between these groups. For all analyses, $P < 0.05$ was considered as statistically significant. χ^2-Test was applied to calculate the associations and significance of the categorical values. A multivariate analysis was applied to establish association between these two groups after controlling for BMI. Correlation curves using Pearson correlation (r) were determined for certain variables in the subgroups of PCOS to further emphasize the strength of correlation. For parameters that were not normally distributed, such as free testosterone and diastolic blood pressure (DBP), Spearman's rank correlation coefficient was used instead of Pearson's correlation.

Table 1
Patient characteristics.

Parameters	PCOS with SDB (group 1, $n = 33$) Mean (±SD)	PCOS without SDB (group 2, $n = 17$) Mean (±SD)	*P*-value
BMI (kg/m^2)	29.8 (3.4)	24.36 (2.29)	<0.001
Waist circumference (cm)	95.58 (6.47)	85.12 (4.34)	<0.001
SBP (mmHg)	129.27 (10.93)	119.18 (8.03)	0.002
DBP (mmHg)	78.61 (9.07)	73.53 (6.22)	0.044
Ferriman–Gallwey score	9.82 (2.78)	8.00 (2.5)	0.028

PCOS, polycystic ovary syndrome; SDB, sleep-disordered breathing; SD, standard deviation; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure.

3. Results

Fifty women with PCOS participated in this study. On the basis of the PSG findings, 33 (66%) women were diagnosed with SDB. Demographic and clinical characteristics of women with PCOS and SDB (group 1) as well as women having PCOS without SDB (group 2) are shown in Table 1. BMI and waist circumference of women in group 1 were significantly higher than those in group 2 ($P < 0.001$ in both). Further, 81.8% of women in group 1 and only 17.6% of women in group 2 had a waist circumference >88 cm, which is one of the components of MBS. Women in group 1 also had significantly higher systolic blood pressure (SBP) and DBP as compared to those in group 2 ($P = 0.002$ for SBP; $P = 0.044$ for DBP). Of the women in group 1, 12.1% had BP ≥130/85 mmHg, which is another component of MBS, whereas none from group 2 met the criteria. On comparing the mean FG score, a clinical measure of hirsutism, it was seen that patients in group 1 had a significantly higher score ($P = 0.028$), implying that the women having PCOS with SDB were experiencing more severe features of hyperandrogenism.

Table 2 shows the comparison of the metabolic parameters between the two groups. Fasting blood sugar (FBS) level was significantly higher in group 1 than that in group 2 (100.91 ± 21.82 vs 84.35 ± 11.95 mg/dL, $P = 0.006$). Though mean fasting insulin levels and HOMA scores were higher in group 1, they did not reach the level of significance. It was observed that 27.3% of women having PCOS with SDB had an FBS level greater than the cut-off value of 110 mg/dL, which is the third component of MBS, whereas none of the women having PCOS without SDB had such values, and consequently the association was also significant ($P = 0.0174$). On comparison of the level of dyslipidemia between the two subgroups of PCOS, it was found that triglyceride levels were significantly higher in group 1 than in group 2 ($P = 0.014$) whereas HDL levels were significantly lower in the first group ($P = 0.006$), but there were no significant differences in the measures of LDL and cholesterol between the two groups. While taking into consideration the other two components of MBS, that is, HDL <50 mg/dL and TG >150 mg/dL, it was observed that 13 of the 33 cases of PCOS with SDB (39.4%) and only two of the cases of PCOS without SDB (11.8%) exceeded the cut-off levels for triglycerides ($P = 0.043$). Again, 17 (51.5%) patients from group 1 and only one (5.9%) from group 2 were found to have HDL < 50 mg/dL ($P = 0.001$). Although free testosterone and DHEAS levels were higher in group 1 compared to group 2, they did not reach statistical significance. Similarly, mean SHBG values were lower in group 1 compared with group 2. It was observed that 42.4% patients of group 1 and only 11.8% of group 2 had three or more factors out of the five components, which defines MBS that was significantly higher ($P < 0.001$).

Table 2
Comparison of metabolic parameters.

Parameters	PCOS with SDB (group 1, $n = 33$) Mean (±SD)	PCOS without SDB (group 2, $n = 17$) Mean (±SD)	*P*-value
FBS (mg/dL)	100.91 (21.82)	84.35 (11.95)	0.006
Fasting insulin (μU/mL)	23.09 (13.11)	19.03 (10.62)	0.227
HOMA	6.24 (4.28)	4.04 (2.44)	0.057
Triglyceride (mg/dL)	140.30 (36.00)	114.29 (30.52)	0.014
HDL (mg/dL)	50.67 (13.82)	60.35 (9.44)	0.006
LDL (mg/dL)	140.03 (50.86)	127.12 (19.40)	0.204
Cholesterol (mg/dL)	229.27 (66.47)	203.88 (46.92)	0.125
Free testosterone (ng/mL)	3.43 (3.78)	2.01 (2.47)	0.167
DHEAS (μg/dL)	160.77 (111.03)	124.80 (76.99)	0.239
SHBG (ng/mL)	58.06 (38.92)	88.60 (96.94)	0.118
No. of patients with metabolic syndrome	14 (42.4%)	2 (11.8%)	<0.001

PCOS, polycystic ovary syndrome; SDB, sleep-disordered breathing; SD, standard deviation; FBS, fasting blood sugar; HOMA, homeostatic model assessment; HDL, high-density lipoprotein; LDL, low-density lipoprotein; DHEAS, dehydroepiandrostenedione sulfate; SHBG, sex hormone-binding globulin.

Table 3
Comparison of sleep parameters.

Parameters	PCOS with SDB (group 1, $n = 33$)	PCOS without SDB (group 2, $n = 17$)	*P*-value
Excessive daytime sleepiness	22 (66.7%)	6 (35.3%)	0.04
Restless sleep	7 (21.2%)	2 (11.8%)	0.69
Unrefreshing sleep	17 (51.5%)	9 (52.9%)	0.99
Witnessed apneic episodes during sleep	2 (6.1%)	0	
Nocturia	10 (30.3%)	6 (35.3%)	0.76

PCOS, polycystic ovary syndrome; SDB, sleep-disordered breathing.

Parameters of sleepiness in the two groups are shown in Table 3. Prevalence of EDS was significantly higher in group 1 compared to that in group 2 (66.7% vs 35.3%, $P = 0.04$).

RDI significantly correlated with waist circumference ($r = 0.551$, $P < 0.001$) (Fig. 1), SBP ($r = 0.455$, $P = 0.001$) (Fig. 2), and DBP ($r = 0.387$, $P = 0.006$) (Fig. 3). Further, it can be seen that the RDI also significantly correlated with FBS ($r = 0.524$, $P = 0.000$) (Fig. 4), HOMA ($r = 0.512$, $P = 0.000$) (Fig. 5), triglycerides ($r = 0.384$, $P = 0.006$) (Fig. 6), and free testosterone ($R = 0.390$, $P = 0.005$) (Fig. 7). RDI was also found to correlate negatively with HDL ($r = -0.555$, $P = 0.001$) (Fig. 8).

Since there was a significant difference in the BMI of the two groups, which could independently affect the values of the metabolic parameters, a logistic regression analysis was applied to adjust

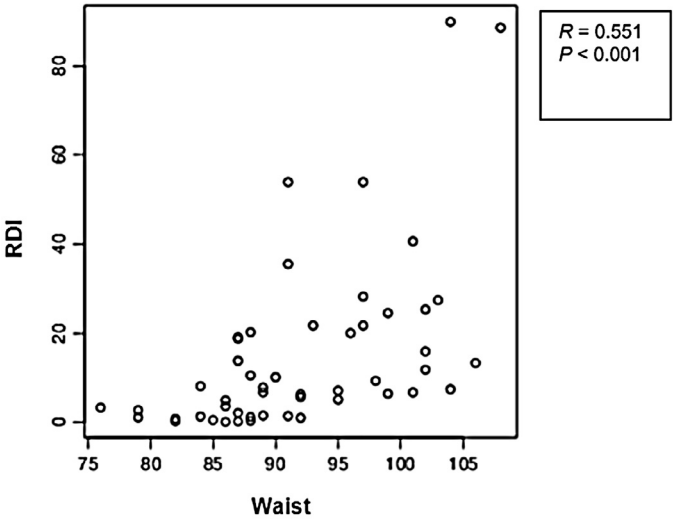

Fig. 1. Correlation between waist circumference and respiratory distress index (RDI) in women with polycystic ovary syndrome and sleep-disordered breathing.

Table 4
Logistic regression of respiratory distress index (RDI) with metabolic parameters.

Metabolic parameters	Standardized coefficient (beta)	*t*	*P*-value
BMI	0.339	2.665	0.011
Waist		0.332	0.741
SBP		–0.215	0.831
DBP		0.569	0.572
FBS	0.28	2.318	0.025
HOMA		1.001	0.322
HDL	–0.254	–2.044	0.047
Triglyceride		0.242	0.810
Free testosterone		1.111	0.273

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBS, fasting blood sugar; HOMA, homeostatic model assessment; HDL, high-density lipoprotein.
Dependent variable: RDI.
Predictors in the model: BMI, FBS, HDL.

for BMI, and it can be seen in Table 4 that SDB was still significantly correlating with HDL and FBS.

4. Discussion

This study was undertaken with the aim of determining the effect of SDB on the metabolic dysfunctions seen in patients with PCOS. In this study, we have shown that there are several anthropometric and metabolic parameters that are significantly deranged in the patients having PCOS with SDB compared with those who do not have SDB.

Hyperandrogenemia is a hallmark and diagnostic criterion for PCOS. Its manifestation may be biochemical in the form of raised free testosterone and DHEAS levels, and reduced levels of SHBG, or as clinical features such as alopecia, acne, and hirsutism [1,26]. In a recent study, it was seen that the circulating levels of testosterone and DHEAS were elevated in 50–75% of patients with PCOS [36]. High levels of testosterone inhibit FSH induction of LH receptors on granulosa cells, hence maturation of dominant follicle is not completed. The androgens have been found to contribute to the pathogenesis of SDB, whereas estrogen and progesterone appear to exert a protective effect [37]. Although studies showing high prevalence of SDB in postmenopausal women affirm the protective role of female hormones, the exact role of androgens remains to be clearly

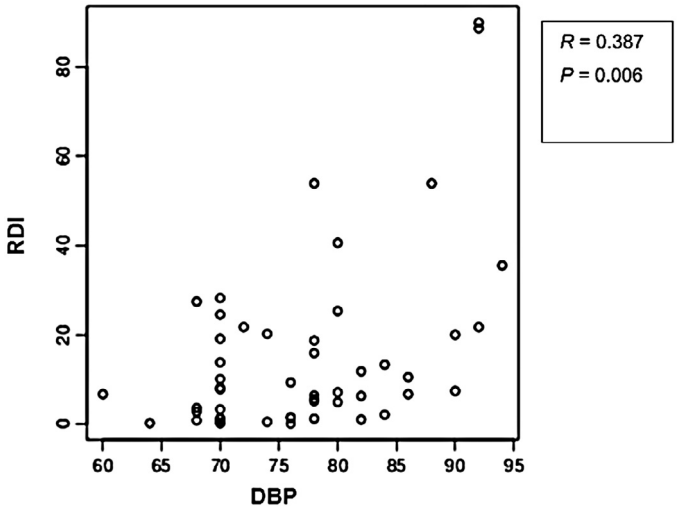

Fig. 3. Correlation between diastolic blood pressure (DBP) and respiratory distress index (RDI) in women with polycystic ovary syndrome and sleep-disordered breathing using Spearman's rank correlation coefficient.

delineated. The fact that SDB is more frequent in men often leads to such assumptions. The adverse effects of menopause and the protective role of gonadal hormones on sleep apnea were shown in the Sleep Heart Health Study [38]. In another study by Liu et al. [39], a positive correlation between severity of SDB and androgens levels was observed. Saaresranta and Polo [40] reported the case of a woman with androgen-secreting ovarian tumor who presented with clinically significant sleep apnea, which disappeared after resection of the tumor. The pathophysiological mechanism by which elevated testosterone levels predispose to develop SDB may be due to increased soft tissue deposition in the pharynx, making it more collapsible during sleep. Testosterone can also exert a major effect on the ventilatory control mechanism, thereby influencing the patency of the pharynx during sleep [41].

It was observed in our study that the levels of free testosterone were higher in group 1 and there was a positive correlation with increasing severity of SDB, implying the strong association of SDB with hyperandrogenemia in patients with PCOS. This was also manifested clinically, as those with both disorders showed greater clinical

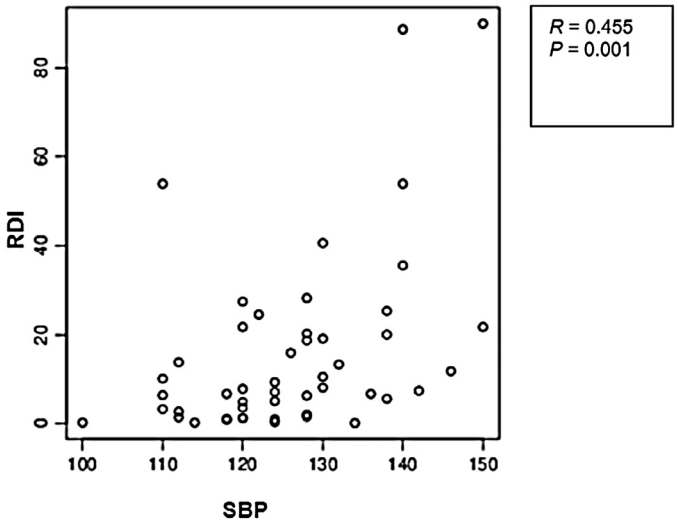

Fig. 2. Correlation between systolic blood pressure (SBP) and respiratory distress index (RDI) in women with polycystic ovary syndrome and sleep-disordered breathing.

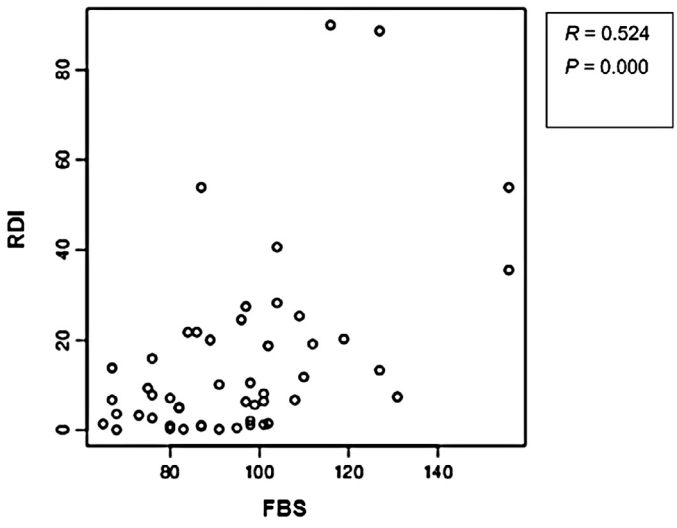

Fig. 4. Correlation between fasting blood sugar (FBS) and respiratory distress index (RDI) in women with polycystic ovary syndrome and sleep-disordered breathing.

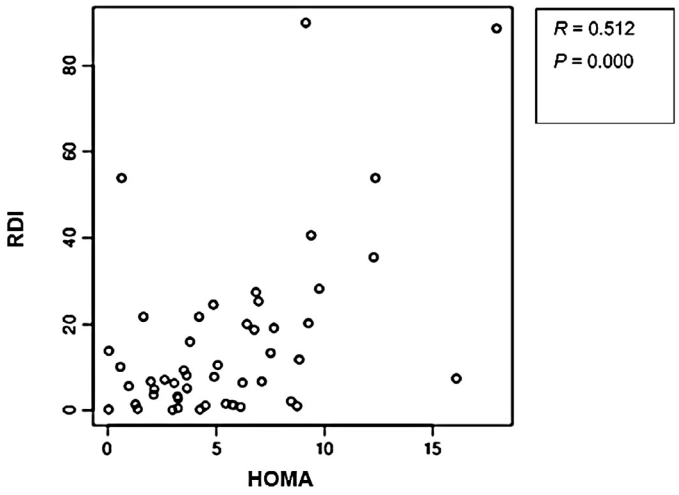

Fig. 5. Correlation between homeostatic model assessment (HOMA) and respiratory distress index (RDI) in women with polycystic ovary syndrome and sleep-disordered breathing.

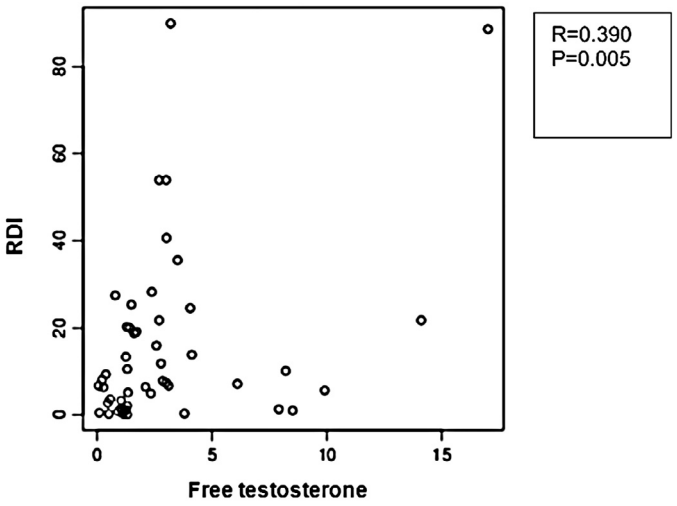

Fig. 7. Correlation between levels of free testosterone and respiratory distress index (RDI) in women with polycystic ovary syndrome and sleep-disordered breathing using Spearman's rank correlation coefficient.

features of hyperandrogenism such as hirsutism, acne, and alopecia – a finding corroborated by other studies [42].

IR is another defining feature of PCOS and is present in ~60–70% cases of PCOS [43]. Hyperinsulinemia directly stimulates ovarian theca cells resulting in increased androgen production. In addition, it potentiates action of LH [6,7], decreases liver production of SHBG, and hence increases androgen levels [4,8]. In other studies, IR has also been incriminated in the development of SDB, and a positive correlation between IR and SDB has been observed [44,45]. In our study, we also found that FBS was significantly higher in patients having PCOS with SDB. Though fasting insulin and HOMA scores were higher in this group, the difference was not statistically significant. However, the HOMA score correlated positively with increasing values of RDI. This suggests a strong association between IR and SDB, though further studies in this direction are required to elucidate the exact relationship.

Abnormalities in lipid profile are a well-established sequel in both PCOS and SDB [22]. In the present study, as hypothesized, patients with both PCOS and SDB had significantly raised TG and lowered HDL levels compared to those PCOS patients without SDB. A positive correlation was observed between the TG levels and severity of SDB (RDI). Similarly, a negative correlation was observed between HDL values and RDI. When other parameters of MBS were taken into account, we saw in our study that not only was the mean waist circumference higher in group 1, but also it correlated positively with increasing severity of SDB. Waist circumference, which is taken as a marker for central adiposity, has been found to be significantly raised in other studies [46–49]. Hyperandrogenism and IR have been largely implicated in the development of central obesity in these patients. This may also be one of the important contributory factors in the development of SDB in patients with PCOS.

There was a significant difference in the BMI of the two groups in our study. As BMI is an independent risk factor for development of SDB, we applied logistic regression analysis to adjust for the BMI. Even after adjustment, the severity of SDB correlated significantly with FBS and HDL levels in women with PCOS and SDB.

It was observed in our study that the mean SBP and DBP levels were significantly higher in group 1 than those in group 2. The fact that SBP and DBP correlated positively with rising values of RDI may

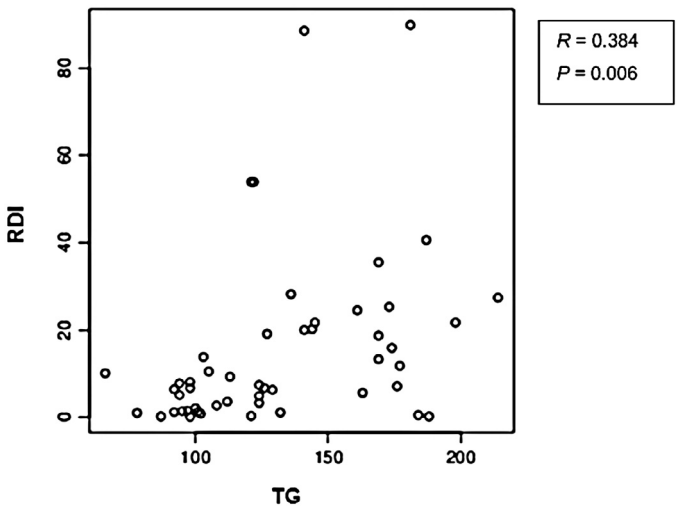

Fig. 6. Correlation between triglyceride (TG) levels and respiratory distress index (RDI) in women with polycystic ovary syndrome and sleep-disordered breathing.

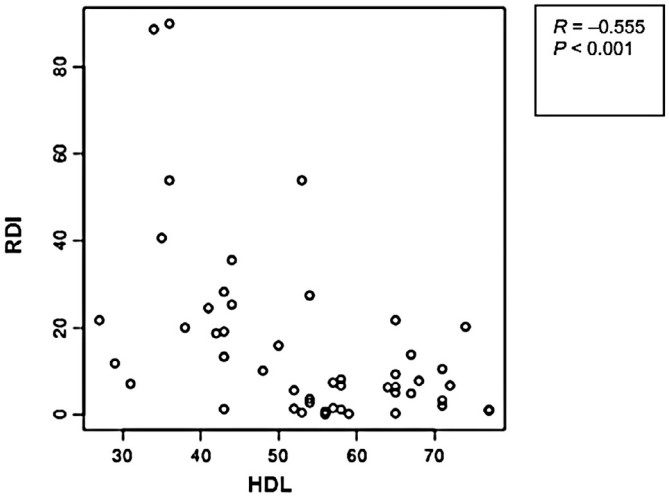

Fig. 8. Correlation between high-density lipoprotein (HDL) levels and respiratory distress index (RDI) in women with polycystic ovary syndrome and sleep-disordered breathing.

indicate that SDB contributes significantly to the development of hypertension in these patients.

From the above findings, it appears that there is a strong association between PCOS and SDB. However, it is difficult to establish the exact cause–effect relationship. It appears that biochemical abnormalities, such as hyperandrogenism and IR, observed in patients with PCOS, predispose these patients to develop SDB, and then SDB in turn aggravates these biochemical and metabolic abnormalities, resulting in a vicious cycle. As observed in SDB patients in the general population, there is significant increase in the prevalence of hypertension, IR, lipid abnormalities, strokes, and IHD. It has also been observed that treatment with continuous positive airway pressure device results in significant improvement in many of these parameters.

Like SDB patients in the general population, PCOS patients with SDB might also be at increased risk of developing long-term cardiovascular complications if their SDB remains untreated. However, long-term follow-up studies are required to establish these issues.

The limitation of this study was that the study group was relatively small. It was a cross-sectional study on untreated cases of PCOS, and the effect of treatment of PCOS on the severity of SDB could not be determined. Further longitudinal studies are warranted to address this important issue. Interventional studies to determine the impact of treatment of SDB on the clinical and metabolic profiles in women with PCOS will also help to resolve the cause–effect relationship.

We conclude in this study that women with PCOS had significantly increased prevalence of SDB, and that patients having PCOS with SDB had significantly increased metabolic abnormalities as well as more severe hyperandrogenism, which also increased with the severity of SDB. These patients also reported EDS. It is therefore recommended that all women with PCOS should be screened for SDB using a validated sleep questionnaire, and those with high suspicion of SDB should undergo an overnight PSG.

Conflict of interest

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: http://dx.doi.org/10.1016/j.sleep.2014.06.023.

Acknowledgements

We thank Dr Ayan Jha, Scientist Grade C, ICMR, New Delhi, for help in statistical analysis and Miss Shalu Soni for her secretarial help. Our gratitude extends to the colleagues at VMMC and Safdarjung Hospital and, most importantly, to our patients for their co-operation.

References

[1] Ehrmann DA. Medical progress: polycystic ovary syndrome. N Engl J Med 2005;352:1223–36.
[2] Franks S. Polycystic ovary syndrome. N Engl J Med 1995;333:853–61.
[3] Guzick DS. Polycystic ovary syndrome. Obstet Gynecol 2004;103:181–93.
[4] Legro RS. Diagnostic criteria in polycystic ovary syndrome. Semin Reprod Med 2003;21:267–75.
[5] Forrester-Dumont K, Galescu O, Kolesnikov A, Raissouni N, Bhangoo A, Ten S, et al. Hyperandrogenism does not influence metabolic parameters in adolescent girls with PCOS. Int J Endocrinol 2012;2012:434830.
[6] Vgontzas AN, Legro RS, Bixler EO, Grayev A, Kales A, Chrousos GP. Polycystic ovary syndrome is associated with obstructive sleep apnea and daytime sleepiness: role of insulin resistance. J Clin Endocrinol Metab 2001;86:517–20.
[7] Nestler JE, Jakubowicz DJ, de Vargas AF, Brik C, Quintero N, Medina F. Insulin stimulates testosterone biosynthesis by human thecal cells from women with polycystic ovary syndrome by activating its own receptors and using inositolglycan mediators as the signal transduction system. J Clin Endocrinol Metab 1998;83:2001–5.
[8] Tasali E, Van Cauter E, Ehrmann DA. Polycystic ovary syndrome and obstructive sleep apnea. Sleep Med Clin 2008;3:37–46.
[9] Diamanti-Kandarakis E, Kouli CR, Bergiele ET, Filandra FA, Tsianateli TC, Spina GG, et al. A survey of the polycystic ovary syndrome in the Greek Island of Lesbos: hormonal and metabolic profile. J Clin Endocrinol Metab 1999;84:4006–11.
[10] Dunaif A. Hyperandrogenic anovulation (PCOS): a unique disorder of insulin action associated with an increased risk of non-insulin-dependent diabetes mellitus. Am J Med 1995;98:33S–39S.
[11] Ehrmann DA, Barnes RB, Rosenfield RL, Cavaghan MK, Imperial J. Prevalence of impaired glucose tolerance and diabetes in women with polycystic ovary syndrome. Diabetes Care 1999;22:141–6.
[12] Legro RS, Kunselman AR, Dodson WC, Dunaif A. Prevalence and predictors of risk for type 2 diabetes mellitus and impaired glucose tolerance in polycystic ovary syndrome: a prospective controlled study in 254 affected women. J Clin Endocrinol Metab 1999;84:165–9.
[13] Reaven GM. Banting lecture 1988: role of insulin resistance in human disease. Diabetes 1988;37:1595–607.
[14] Reaven GM. Insulin resistance, hyperinsulinemia, hypertriglyceridemia and hypertension: parallels between human disease and rodent models. Diabetes Care 1991;14:195–202.
[15] Zavaroni I, Bonora E, Pagliara M, Dall'Aglio E, Luchetti L, Buonanno G, et al. Risk factors for coronary artery disease in healthy persons with hyperinsulinemia and normal glucose tolerance. N Engl J Med 1989;320:702–6.
[16] American Academy of Sleep Medicine. International classification of sleep disorders: diagnostic and coding manual. 2nd ed. Westchester, IL: AASM; 2005.
[17] Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The occurrence of sleep-disordered breathing among middle aged adults. N Engl J Med 1993;328:1230–5.
[18] Kim J, In K, Kim J, You S, Kang K, Shim J, et al. Prevalence of sleep disordered breathing in middle aged Korean men and women. Am J Respir Crit Care Med 2004;170:1108–13.
[19] Shinohara E, Kihara S, Yamashita S, Yamane M, Nishida M, Arai T, et al. Visceral fat accumulation as an important risk factor for obstructive sleep apnoea syndrome in obese subjects. J Intern Med 1997;241:11–18.
[20] Liu K, Yee B, Philips C, Grunstein RR. Sleep apnea and neuroendocrine function. Sleep Med Clin 2007;2:225–36.
[21] Bixler EO, Vgontzas A, Lin HM, Ten Have T, Rein J, Vela-Bueno A, et al. Prevalence of sleep disordered breathing in women: effects of gender. Am J Respir Crit Care Med 2001;163:608–13.
[22] Peppard PE, Young T, Palta M, Skatrud J. Prospective study of the association of sleep disordered breathing and hypertension. N Engl J Med 2000;342:1378–84.
[23] Redline S, Yenokyan G, Gottlieb DJ, Shahar E, O'Connor GT, Resnick HE, et al. Obstructive sleep apnea–hypopnea and incident stroke: the Sleep Heart Health Study. Am J Respir Crit Care Med 2010;182:269–77.
[24] Coughlin SR, Mawdsley L, Mugarza JA, Calverley PMA, Wilding JPH. Obstructive sleep apnea is independently associated with an increased prevalence of metabolic syndrome. Eur Heart J 2004;25:735–41.
[25] Gottlieb DJ, Yenokyan G, Newman AB, O'Connor GT, Punjabi NM, Quan SF, et al. Prospective study of obstructive sleep apnea and incident coronary heart disease and heart failure: the Sleep Heart Health Study. Circulation 2010;122:352–60.
[26] Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long term health risk related to polycystic ovary syndrome (PCOS). Hum Reprod 2004;19:41–7.
[27] Ferriman D, Gallwey JD. Clinical assessment of body hair growth in women. J Clin Endocrinol Metab 1961;21:1440–7.
[28] Misra A, Chowbey P, Makkar BM, Vikram NK, Wasir JS, Chadha D, et al. Consensus statement for diagnosis of obesity, abdominal obesity and the metabolic syndrome for Asian Indians and recommendations for physical activity, medical and surgical management. J Assoc Physicians India 2009;57:163–70.
[29] John MW. A new method for measuring daytime sleepiness: the Epworth Sleepiness Scale. Sleep 1991;14:540–5.
[30] John MW. Reliability and factor analysis of the Epworth Sleepiness Scale. Sleep 1992;15:376–81.
[31] Johns MW. Sensitivity and specificity of the multiple sleep latency test (MSLT), the maintenance of wakefulness test and the Epworth Sleepiness Scale: failure of the MSLT as a gold standard. J Sleep Res 2000;9:5–11.
[32] Song Y, Manson JE, Tinker L, Howard BV, Kuller LH, Nathan L, et al. Insulin sensitivity and insulin secretion determined by Homeostasis Model Assessment (HOMA) and risk of diabetes in a multiethnic cohort of women: the Women's Health Initiative Observational Study. Diabetes Care 2007;30:1747–52.
[33] McAuley KA, Williams SM, Mann JI, Walker RJ, Lewis-Barned NJ, Temple LA, et al. Diagnosing insulin resistance in general population. Diabetes Care 2001;24:460–4.
[34] National Cholesterol Education Programme (NCEP) Expert Panel. Third report of the national cholesterol education programme (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol (adult treatment panel III) final report. Circulation 2002;106:3143–421.
[35] Iber C, Ancoli-Israel S, Chesson A, Quan SF. The ASSM manual for the scoring of sleep and associated events: rules, terminology and technical specifications. 1st ed. Westchester, IL: American Academy of Sleep Medicine; 2007.
[36] Huang A, Brennan K, Azziz R. Prevalence of hyperandrogenemia in the polycystic ovary syndrome diagnosed by the National Institute of Health 1990 criteria. Fertil Steril 2010;93:1938–41.

[37] Pickett CK, Regensteiner JG, Woodard WD, Hagerman DD, Weil JV, Moore LG. Progestin and estrogen reduce sleep disordered breathing in postmenopausal women. J Appl Physiol 1989;66:1656–61.
[38] O'Connor G, Punjabi N, Quan S, Rapoport D, Redline S, Resnick H, et al. Sleep heart health study (SHHS). ClinicalTrials.gov. 2009. NCT00005275.
[39] Liu PY, Yee B, Wishart SM, Jimenez M, Jung DG, Grunstein RR, et al. The short term effects of high dose testosterone on sleep, breathing and functions in older men. J Clin Endocrinol Metab 2003;88:3605–13.
[40] Saaresranta T, Polo O. Sleep-disordered breathing and hormones. Eur Respir J 2003;22:161–72.
[41] Eckert DJ, Malhotra A. Pathophysiology of adult obstructive sleep apnea. Proc Am Thorac Soc 2008;5:144–53.
[42] Gambineri A, Pelusi C, Vicennati V, Pagotto U, Pasquali R. Obesity and the polycystic ovary syndrome. Int J Obes Relat Metab Disord 2002;26:883–96.
[43] Dunaif A. Insulin resistance and the polycystic ovary syndrome: mechanism and implications for pathogenesis. Endocr Rev 1997;18:774–800.
[44] Ip SM, Lam B, Ng M, Lam WK, Tsang KW, Lam KS. Obstructive sleep apnea is independently associated with insulin resistance. Am J Respir Crit Care Med 2002;165:670–6.
[45] Kassi E, Pervanidou P, Kaltsas G, Chrousos G. Metabolic syndrome: definitions and controversies. BMC Med 2011;9:1–13.
[46] Ricardo A, Woods KS, Reyna R, Key TJ, Knochenhauer ES, Yildiz BO. The prevalence and features of polycystic ovary syndrome in an unselected population. J Clin Endocrinol Metabol 2004;89:2745–9.
[47] Carmelli D, Swan GE, Bliwise DL. Relationship of 30 year changes in obesity to sleep disordered breathing in the Western Collaborative Group Study. Obes Res 2000;8:632–7.
[48] Vgontzas A. Does obesity play a major role in the pathogenesis of sleep apnea and its associated manifestations via inflammation, visceral adiposity, and insulin resistance? Arch Physiol Biochem 2008;114:211–23.
[49] Lecube A, Sampol G, Lloberes P, Romero O, Mesa J, Morell F, et al. Asymptomatic sleep disordered breathing in premenopausal women awaiting bariatric surgery. Obes Surg 2010;20:254–61.